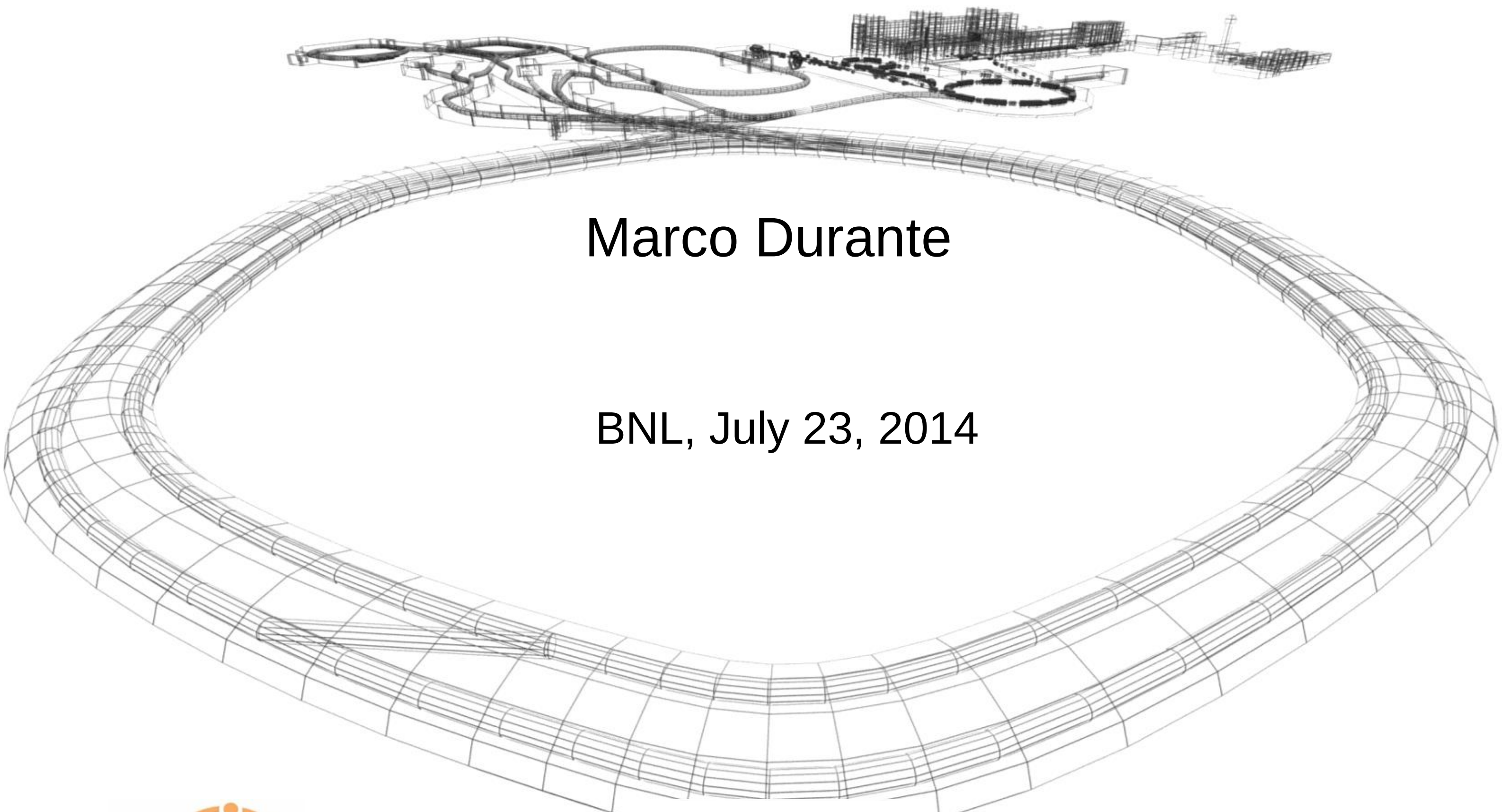
Medical physics for particle therapy

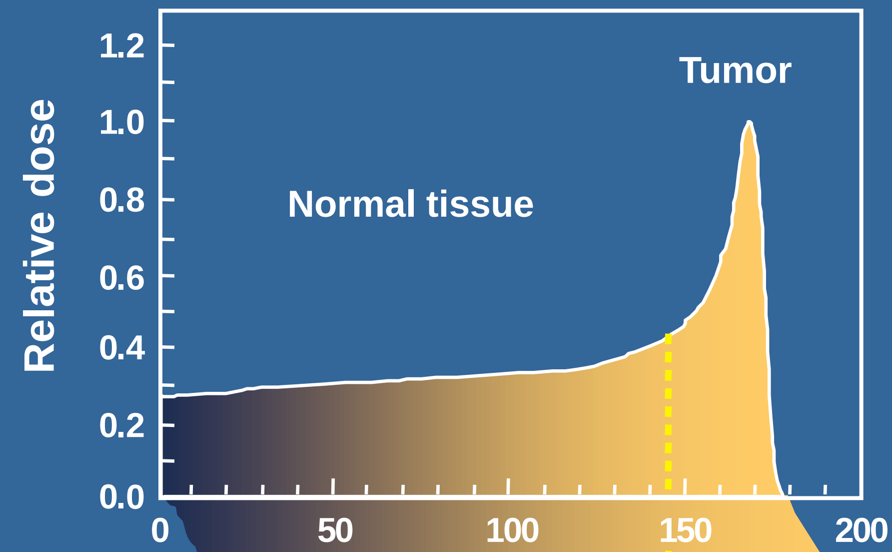


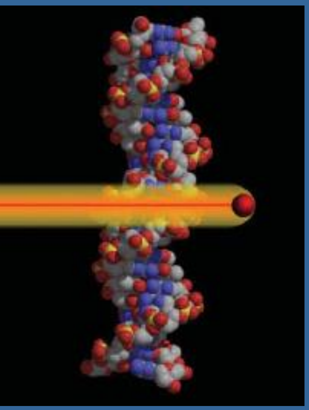
Marco Durante

BNL, July 23, 2014

Durante & Loeffler,

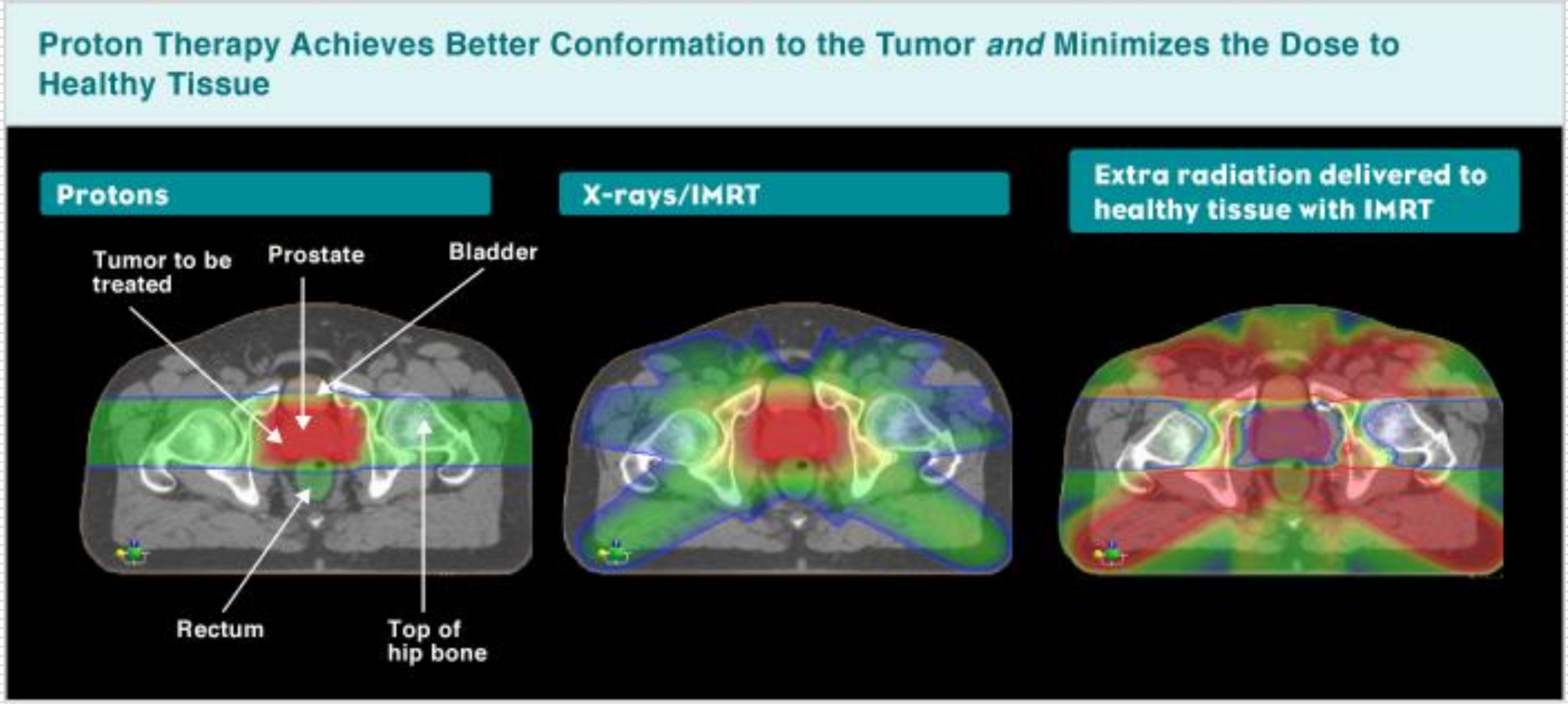
***Nature Rev Clin Oncol* 2010**





			Potential advantages
Energy	high	low	
LET	low	high	
Dose	low	high	High tumor dose, normal tissue sparing
RBE	≈ 1	> 1	Effective for radioresistant tumors
OER	≈ 3	< 3	Effective against hypoxic tumor cells
Cell-cycle dependence	high	low	Increased lethality in the target because cells in radioresistant (S) phase are sensitized
Fractionation dependence	high	low	Fractionation spares normal tissue more than tumor
Angiogenesis	Increased	Decreased	Reduced angiogenesis and metastatization
Cell migration	Increased	Decreased	

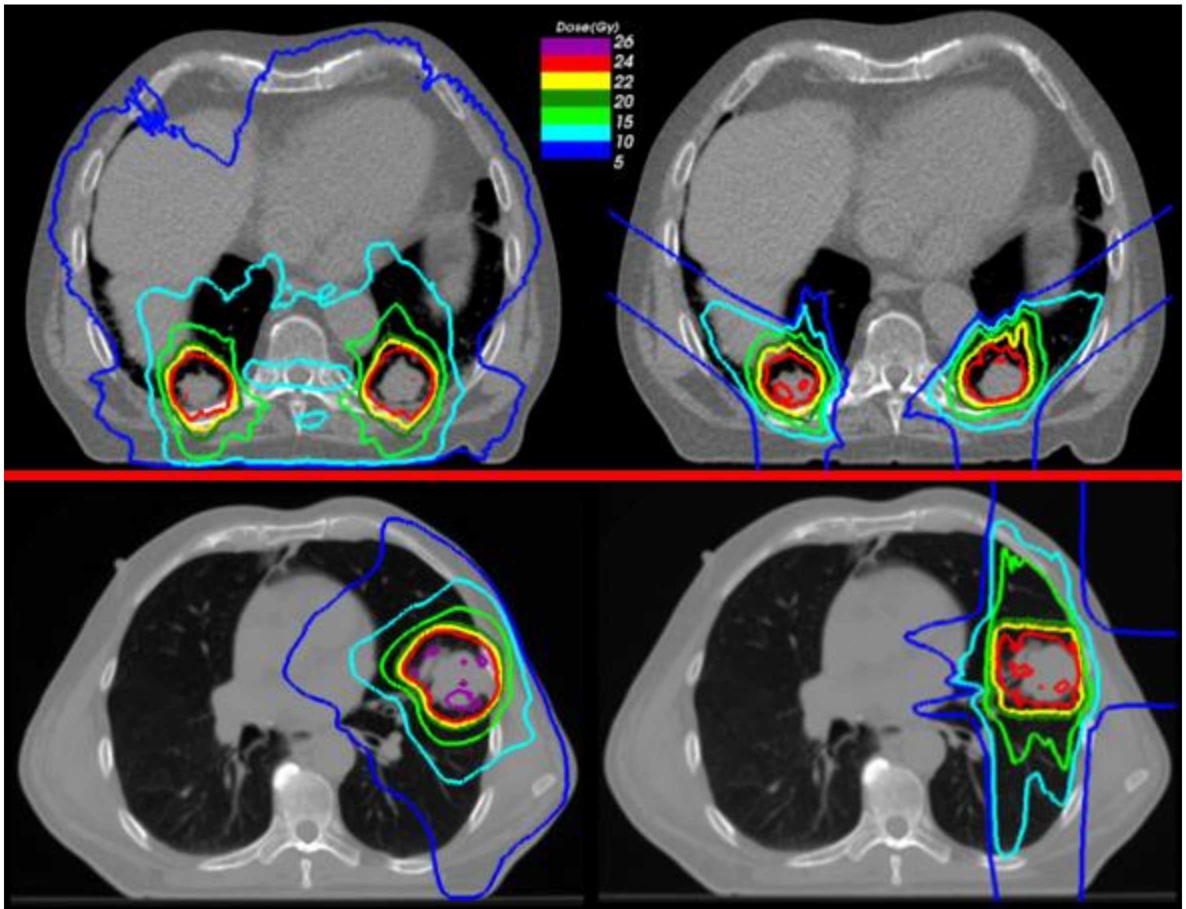
Treatment plans with protons: prostate



Courtesy of Reinhold Schulte, LLUMC

In silico trials
Charged particles vs. SBRT

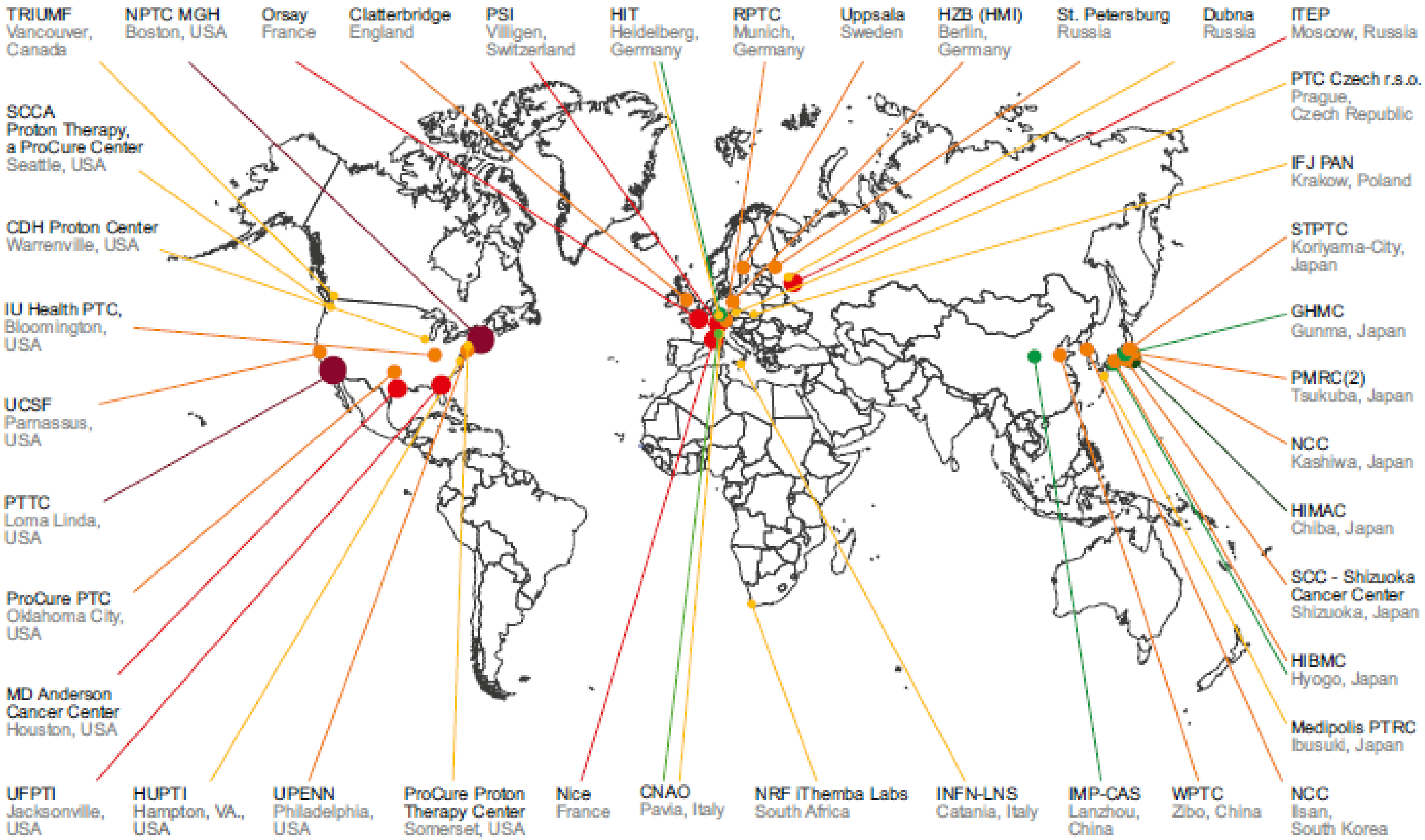
X-rays **Carbon**

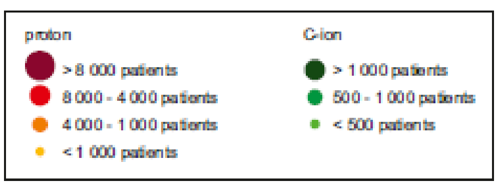


- Patients treated at Champalimaud Foundation, Lisbon (TrueBeam)
- 24 Gy single fx SBRT

In silico trial MSKCC/Champalimaud/ GSI

Christian Anderle, TU Darmstadt, Ph.D. thesis



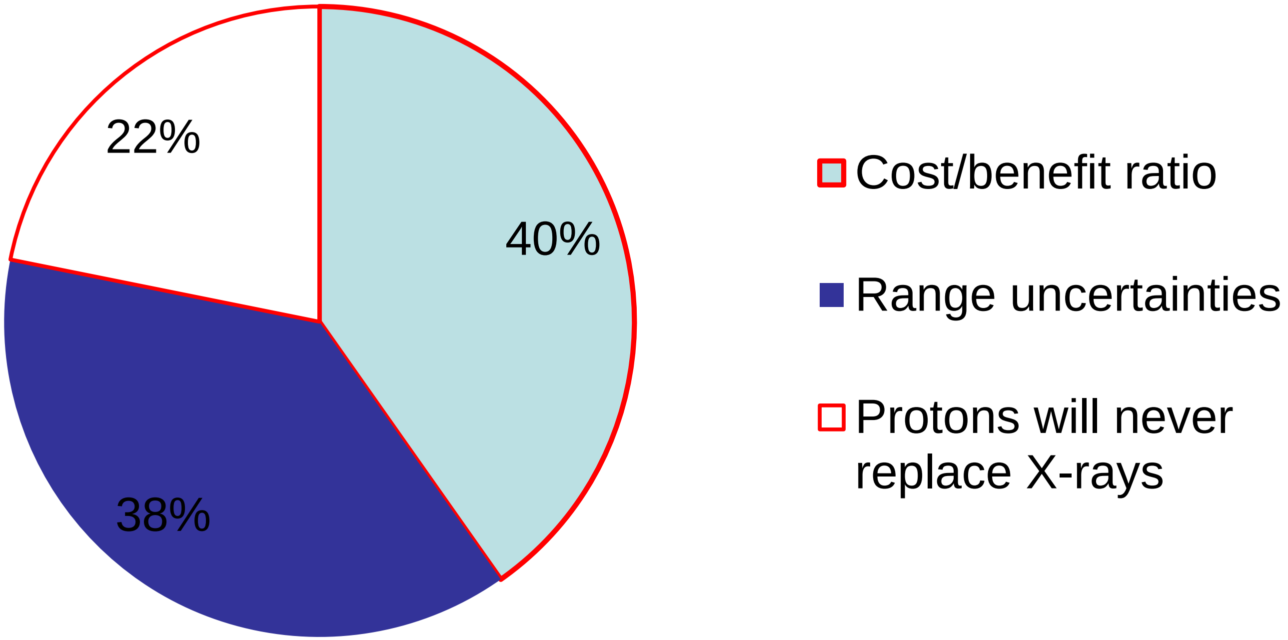


March 2014: 44 proton/7 heavy ion centers
Under construction: 25 proton/ 4 heavy ion centers
Only in USA, 27 new centers expected by 2017

NuPECC report „Nuclear Physics in Medicine“, 2014

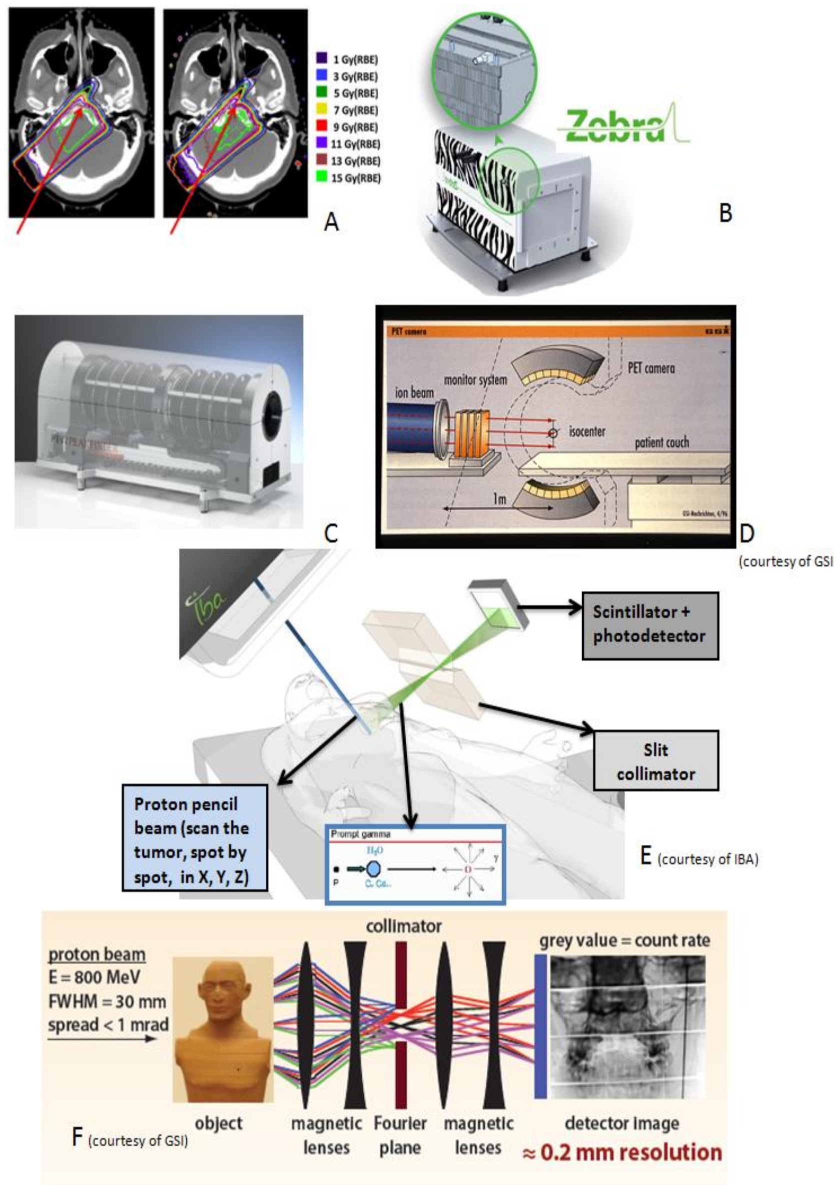
AAPM poll, August 2012

What is the main obstacle to proton therapy replacing X-rays?



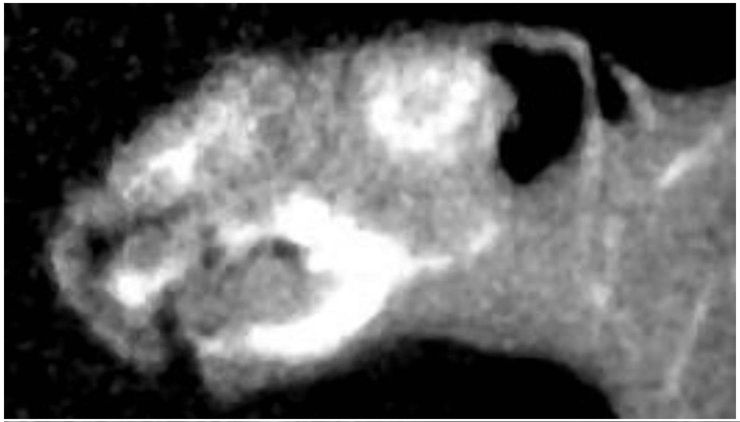
1. Range verification

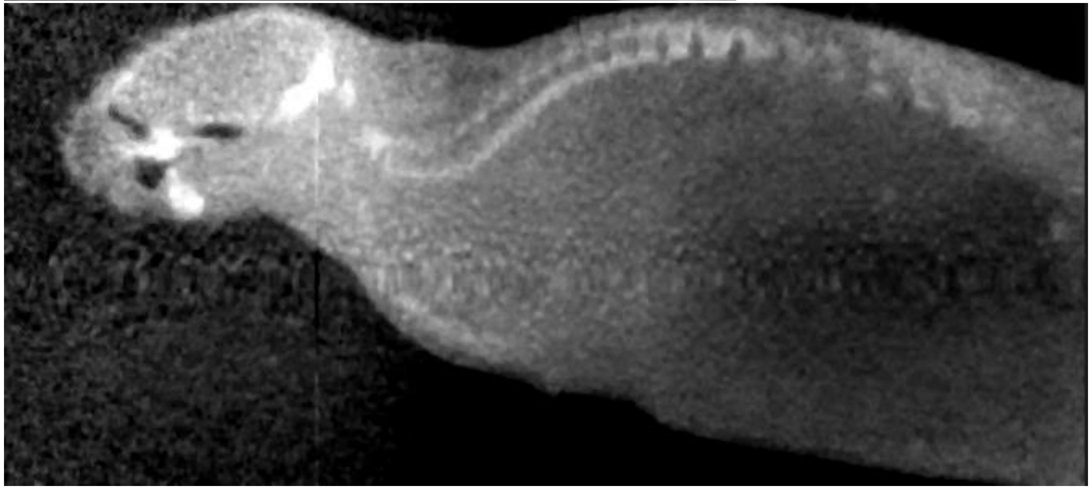
Source of range uncertainty in the patient	Range uncertainty
Independent of dose calculation:	
Measurement uncertainty in water for commissioning	± 0.3 mm
Compensator design	± 0.2 mm
Beam reproducibility	± 0.2 mm
Patient setup	± 0.7 mm
Dose calculation:	
Biology (always positive)	+ 0.8 %
CT imaging and calibration	± 0.5 %
CT conversion to tissue (excluding I-values)	± 0.5 %
CT grid size	± 0.3 %
Mean excitation energies (I-values) in tissue	± 1.5 %
Range degradation; complex inhomogeneities	- 0.7 %
Range degradation; local lateral inhomogeneities *	± 2.5 %
Total (excluding *)	**2.7% + 1.2 mm**
Total	**4.6% + 1.2 mm**



Mouse Proton Tomography

800 MeV proton beam at LANL



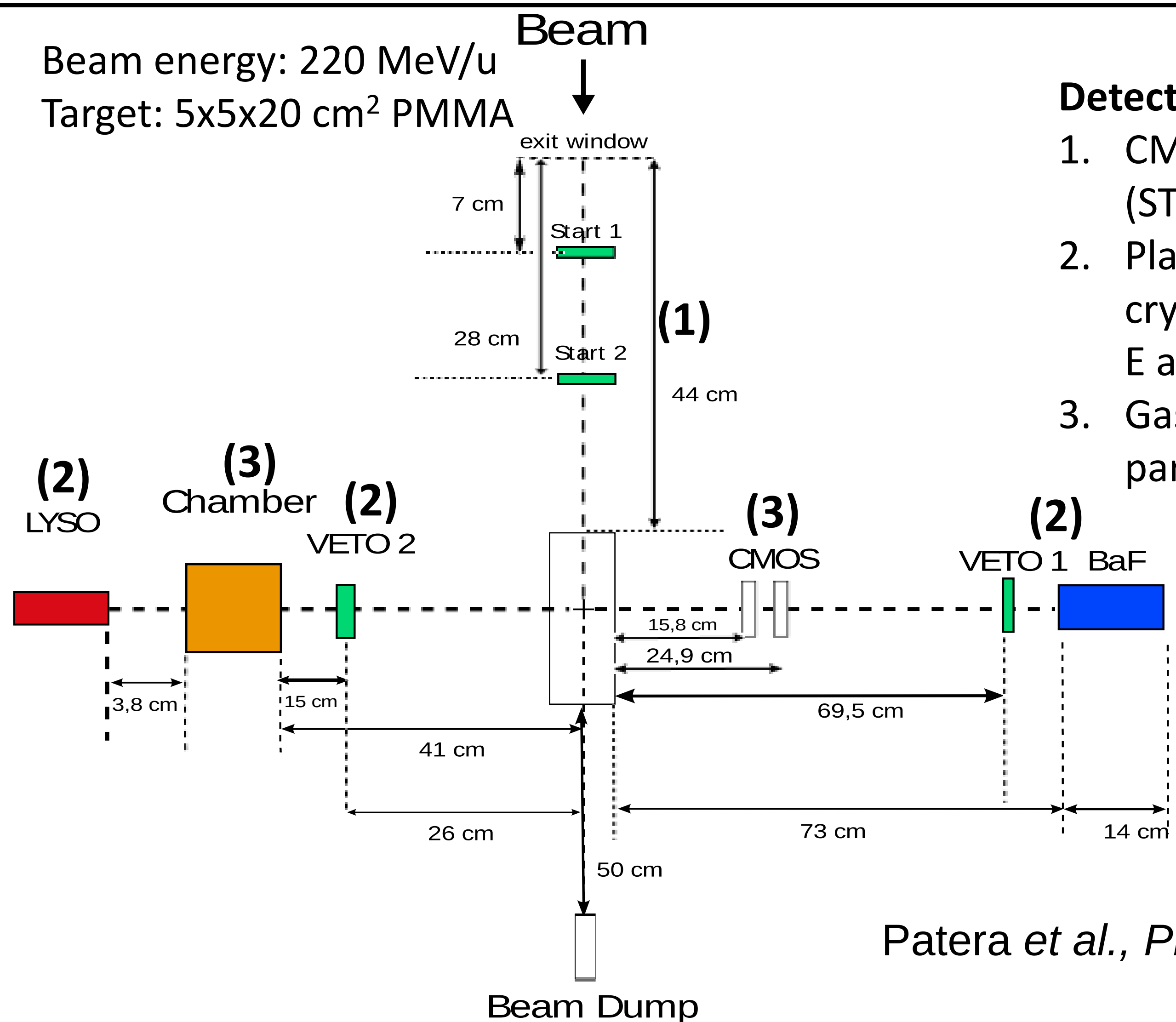


Real time monitoring of the Bragg Peak position during a treatment with ^{12}C beam

Rationale:

Real time, high accuracy (spatial resolution <1 mm)

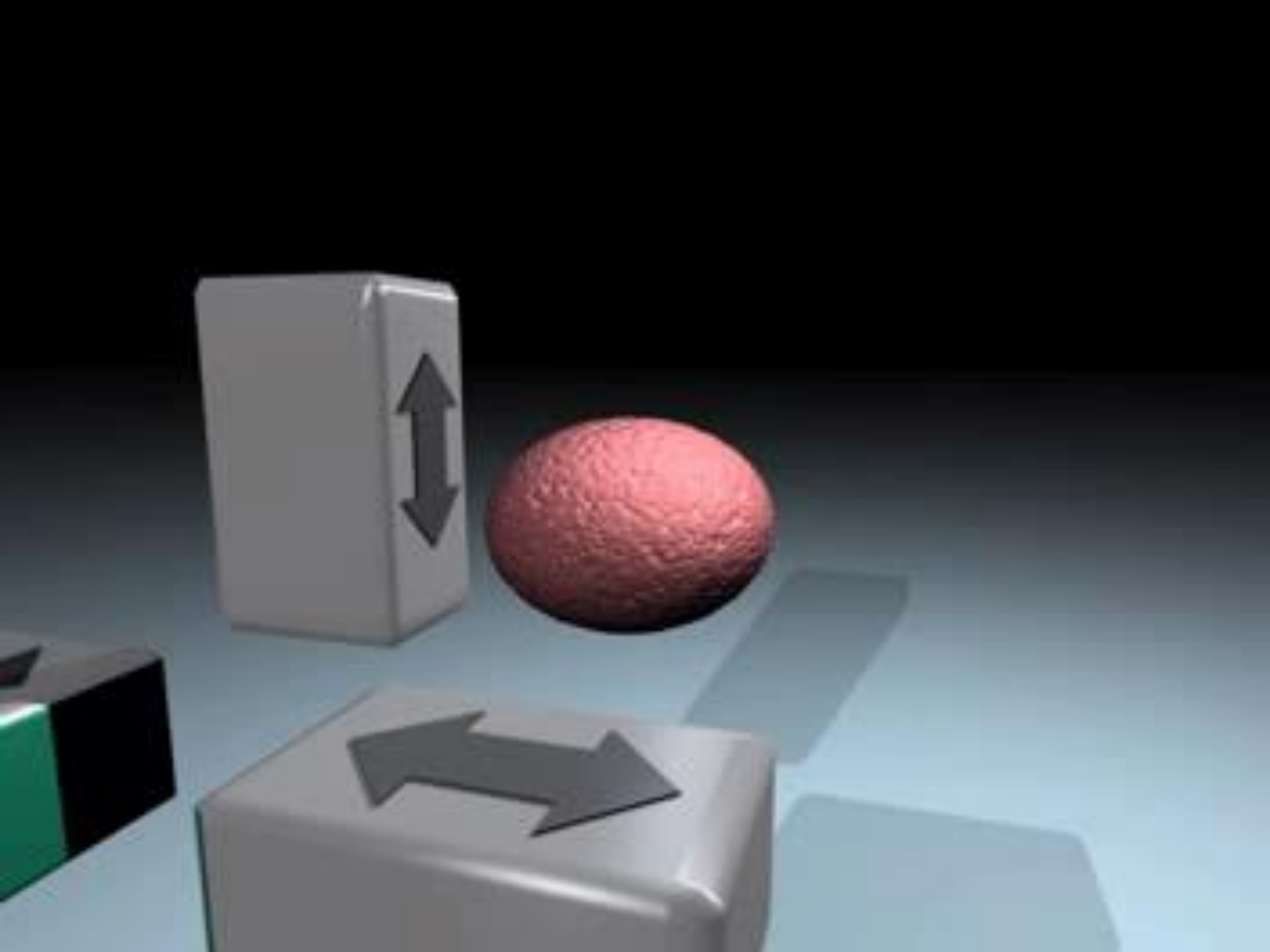
- Beam energy: 220 MeV/u
- Target: 5x5x20 cm^2 PMMA



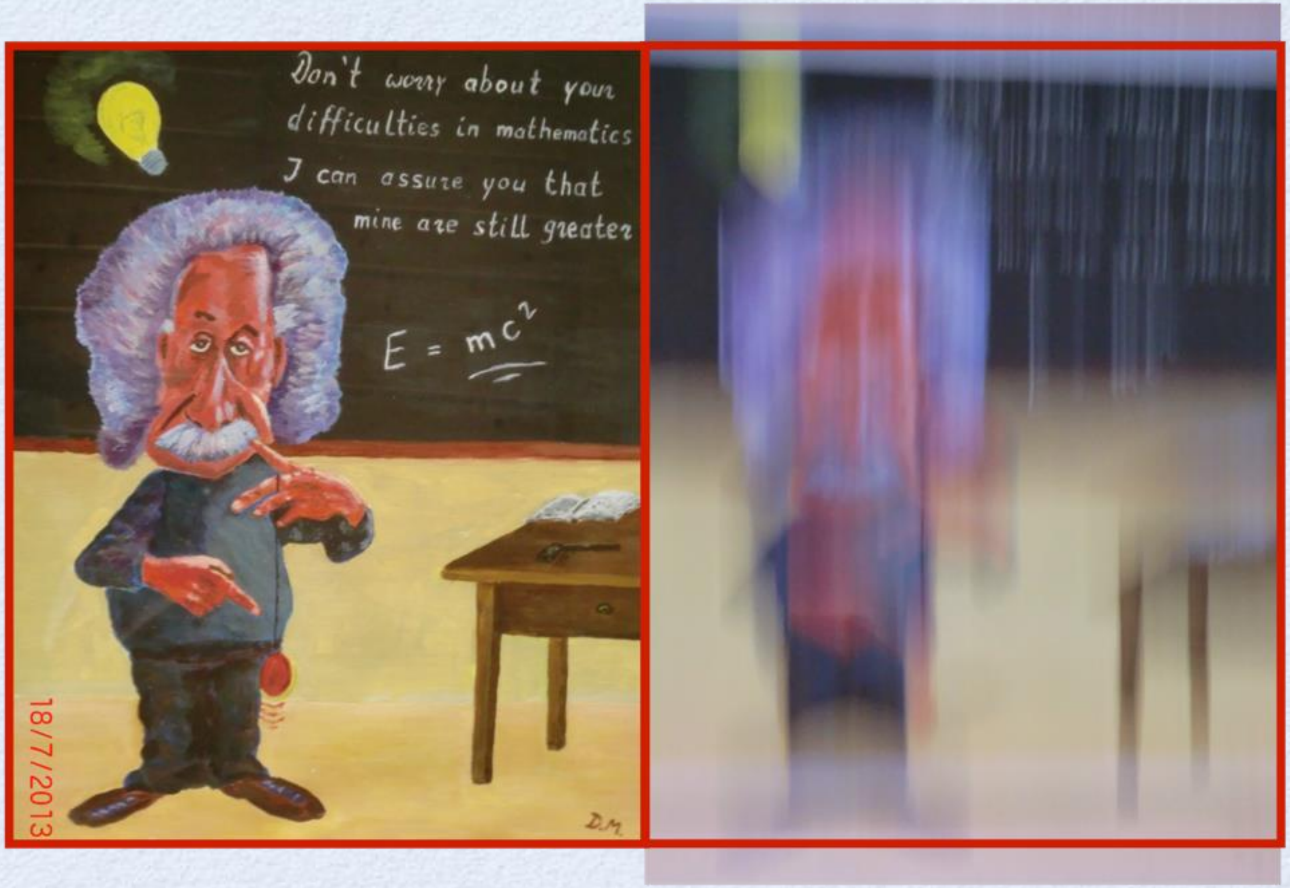
Detectors:

1. CMOS and plastic scintillator (START) for beam monitoring
2. Plastic scintillator (VETO) and crystals (LYSO and BaF) for ΔE-E and TOF measurements
3. Gas chamber and CMOS for particle tracking

Patera *et al.*, *Phys. Med. Biol.* 2014



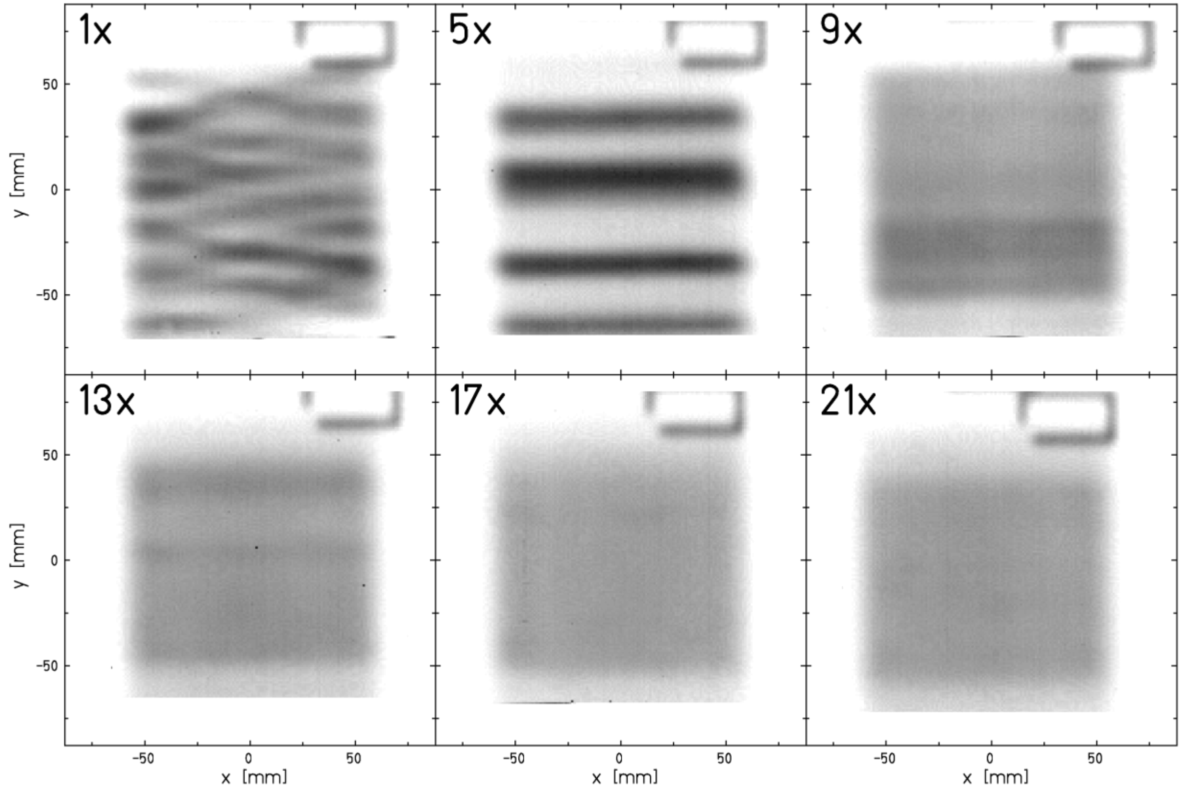
Moving targets: why is motion bad in particle therapy?



Even brilliant Einstein looses brilliance!

Motion mitigation techniques

- **Rescanning**: N irradiations with 1/N dose



- **Gating**
- **Tracking**

Bert & Durante, *Phys. Med. Biol*. 2011

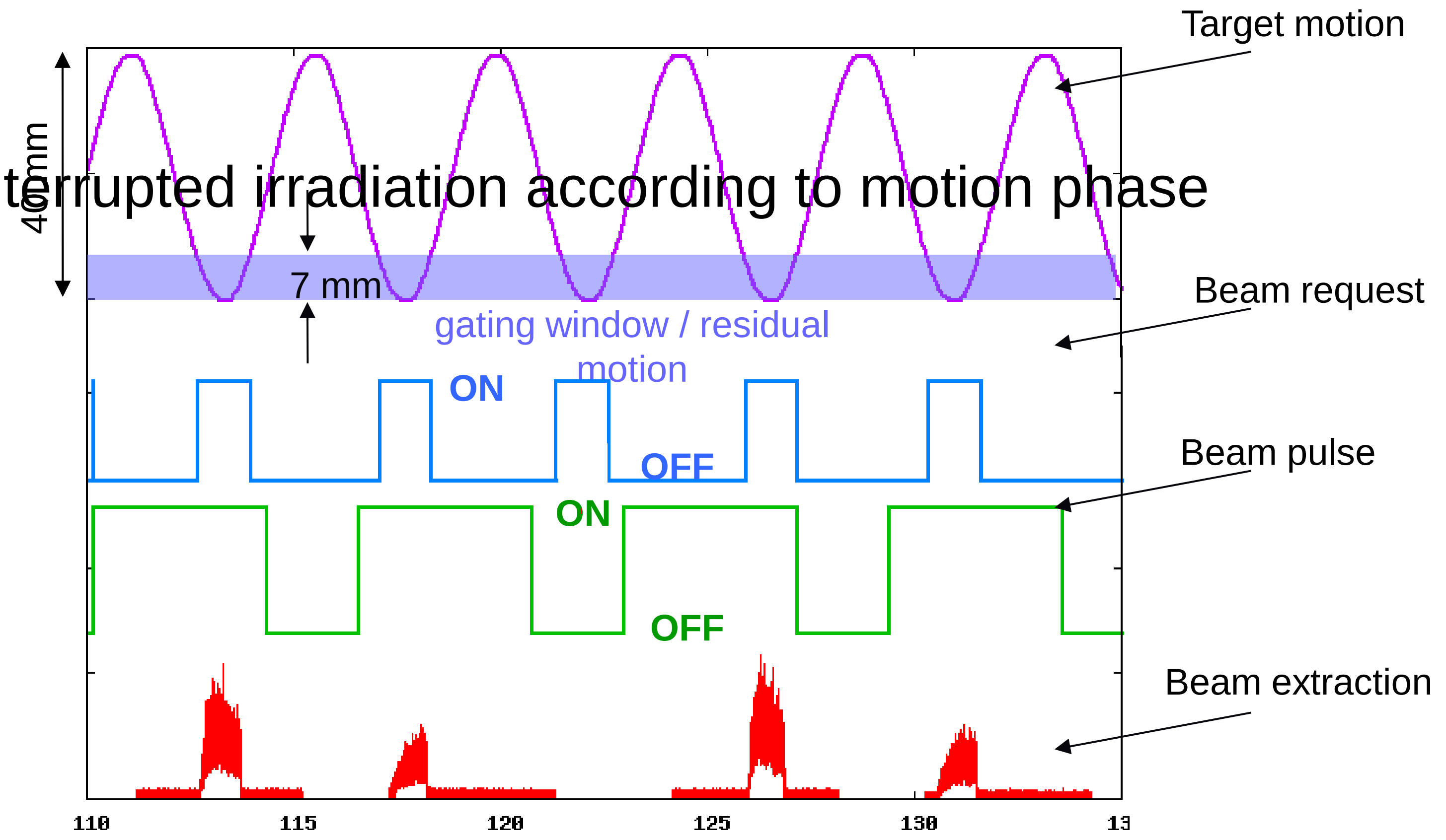
GSI

Motion mitigation techniques

- **Rescanning**: N irradiations with 1/N dose

- **Gating**: interrupted irradiation according to motion phase

- **Tracking**



Bert & Durante, *Phys. Med. Biol*. 2011

GSI

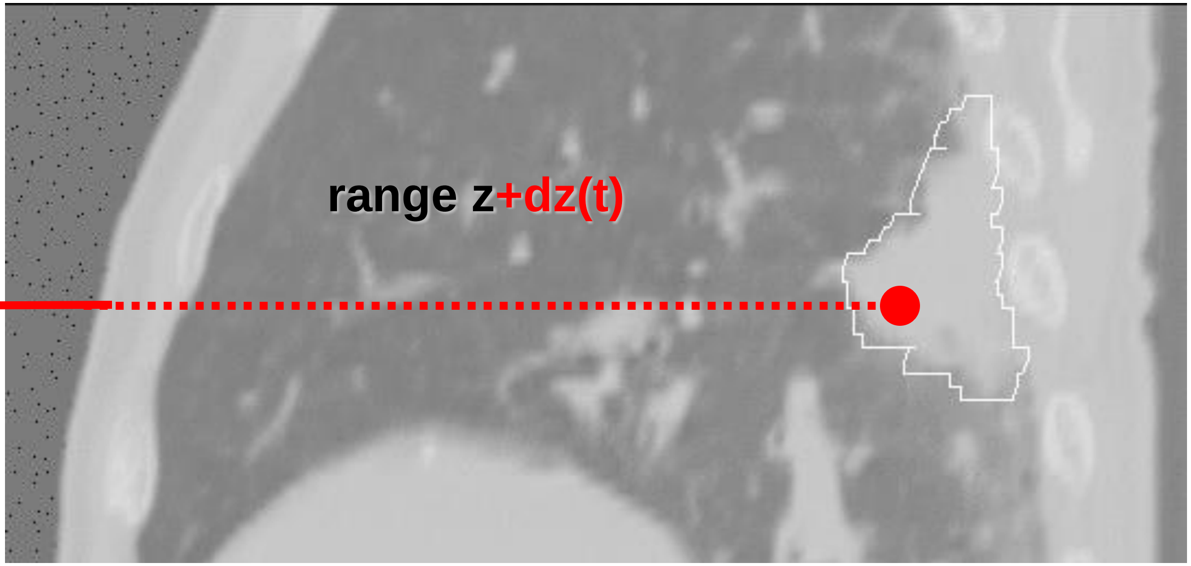
Motion mitigation techniques

- **Rescanning**: N irradiations with 1/N dose

- **Gating**: interrupted irradiation according to motion phase

- **Tracking**

  lateral beam position
  x+dx(t)
  y+dy(t)



Bert & Durante, *Phys. Med. Biol*. 2011

Range uncertainties: tumor tracking in particle therapy

Treatment planning
- 4D CT

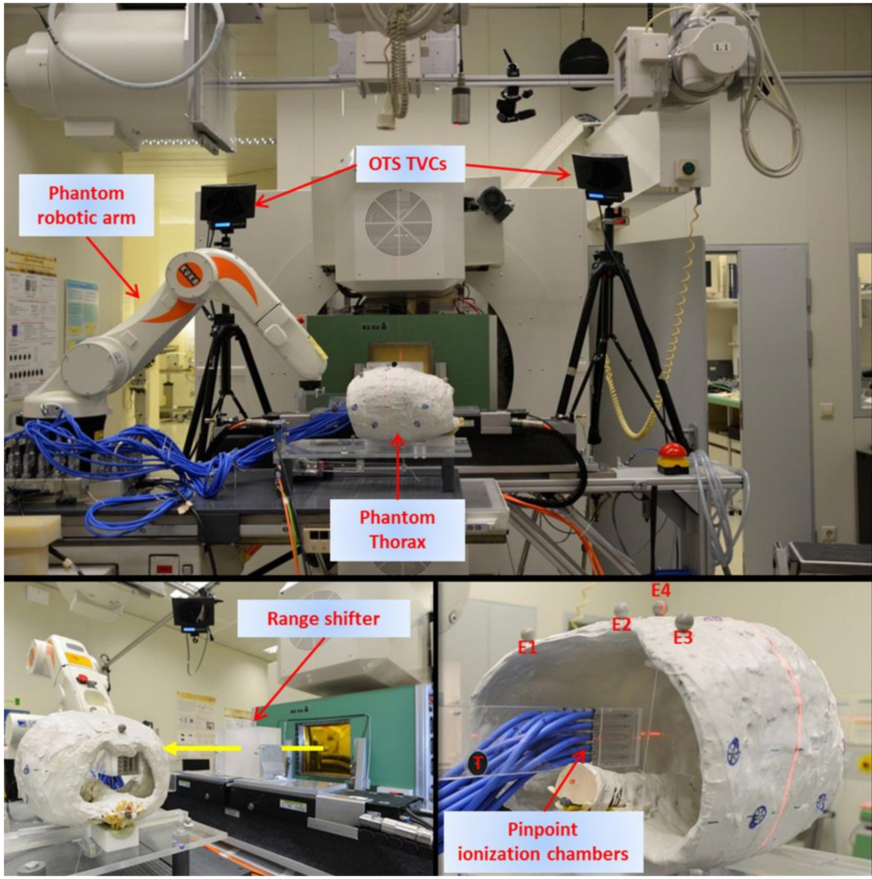
Motion detection
- X-ray stereo projections
- External surrogates combined with adaptive correlation models
- Soft-tissue imaging (ultrasound, MRI)
- Particle radiography

Motion tracking
- Lateral compensation (magnet steering)
- Depth compensation (moving degrader vs static degrader)

Treatment verification
- Off-line PET dosimetry
- In-beam PET dosimetry
- Prompt radiation measurement

Riboldi *et al.*, *Lancet Oncol*. 2012

External-internal correlation model



Seregni *et al.*, *Phys. Med. Biol.* 2013

2. Cost/benefit ratio: new clinical indications

Established clinical indications

- Skull base and spine tumors
- Hepatocellular carcinoma
- Eye tumors
- Pediatric tumors

More research needed for

- Thoracic malignancies
- Head and Neck tumors
- Pelvic and abdominal sites

ASTRO Model Policy, May 2014

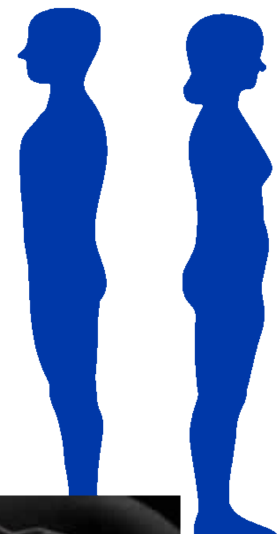
Medulloblastoma treatment, MD Anderson Cencer Center, USA

New diseases where charged particles may potentially lead to a breakthrough

- Lung
- Pancreas
- Local recurrence of rectal cancer
- Breast
- Glioblastoma

Estimated Cancer Deaths in the US in 2013

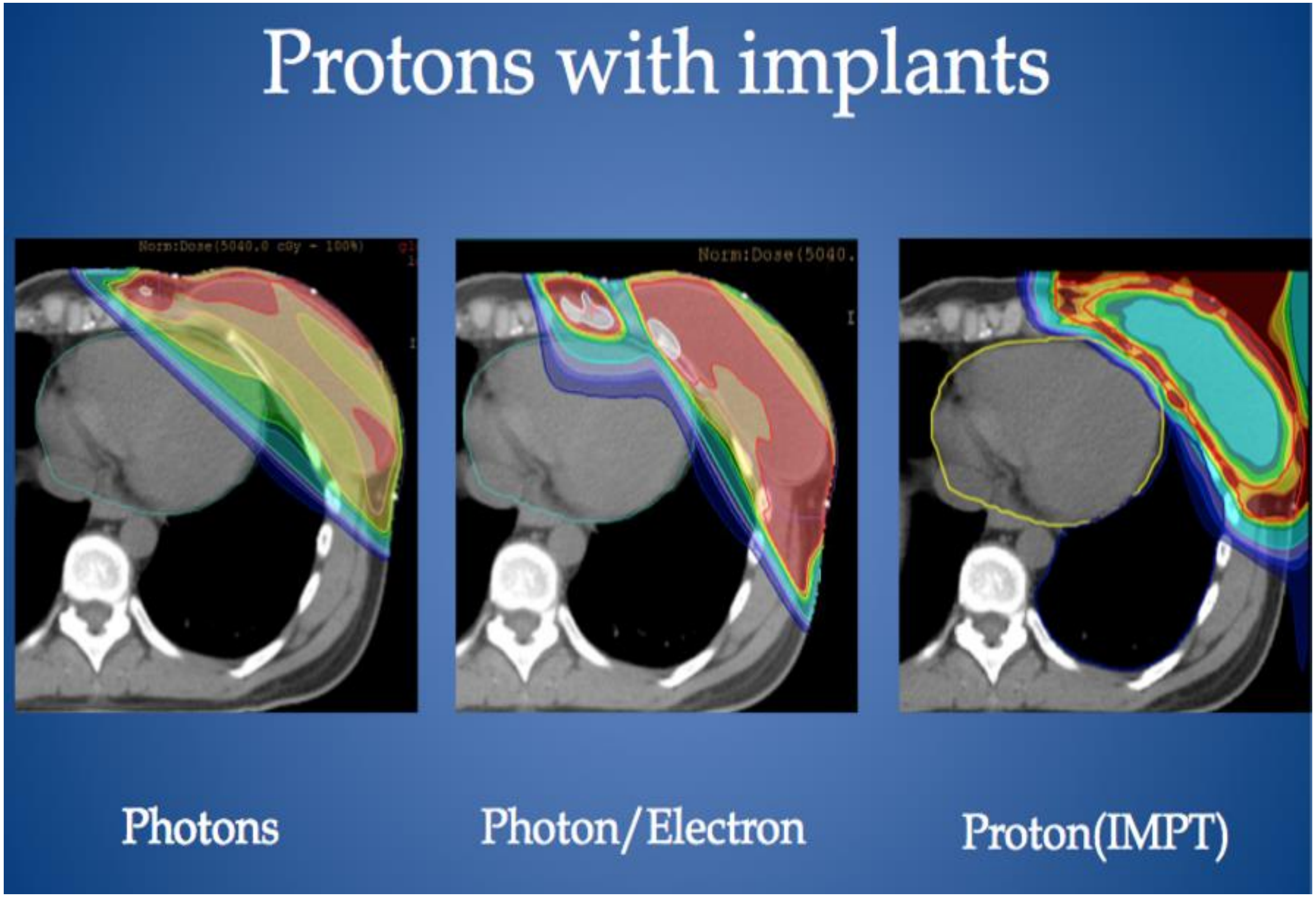
Men 306,920		Women 273,430	
Lung & bronchus	28%	26%	Lung & bronchus
Prostate	10%	14%	Breast
Colon & rectum	9%	9%	Colon & rectum
Pancreas	6%	7%	Pancreas
Liver & intrahepatic bile duct	5%	5%	Ovary
Leukemia	4%	4%	Leukemia
Esophagus	4%	3%	Non-Hodgkin lymphoma
Urinary bladder	4%	3%	Uterine corpus
Non-Hodgkin lymphoma	3%	2%	Liver & intrahepatic bile duct
Kidney & renal pelvis	3%	2%	Brain/other nervous system
All other sites	24%	25%	All other sites



Siegel *et al.*,
CA Cancer J Clin 2013

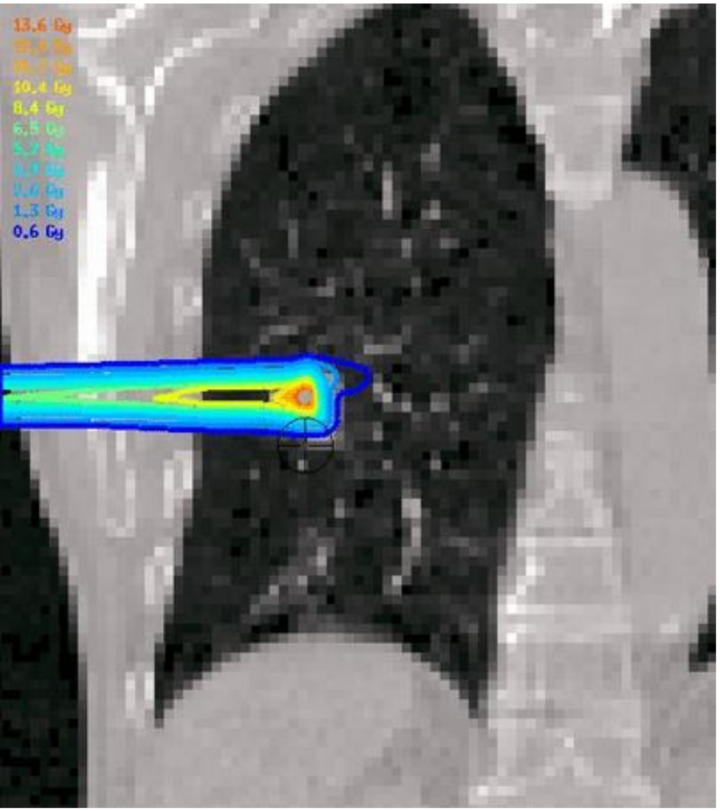
Noncancer diseases

Treatment plans with protons: breast

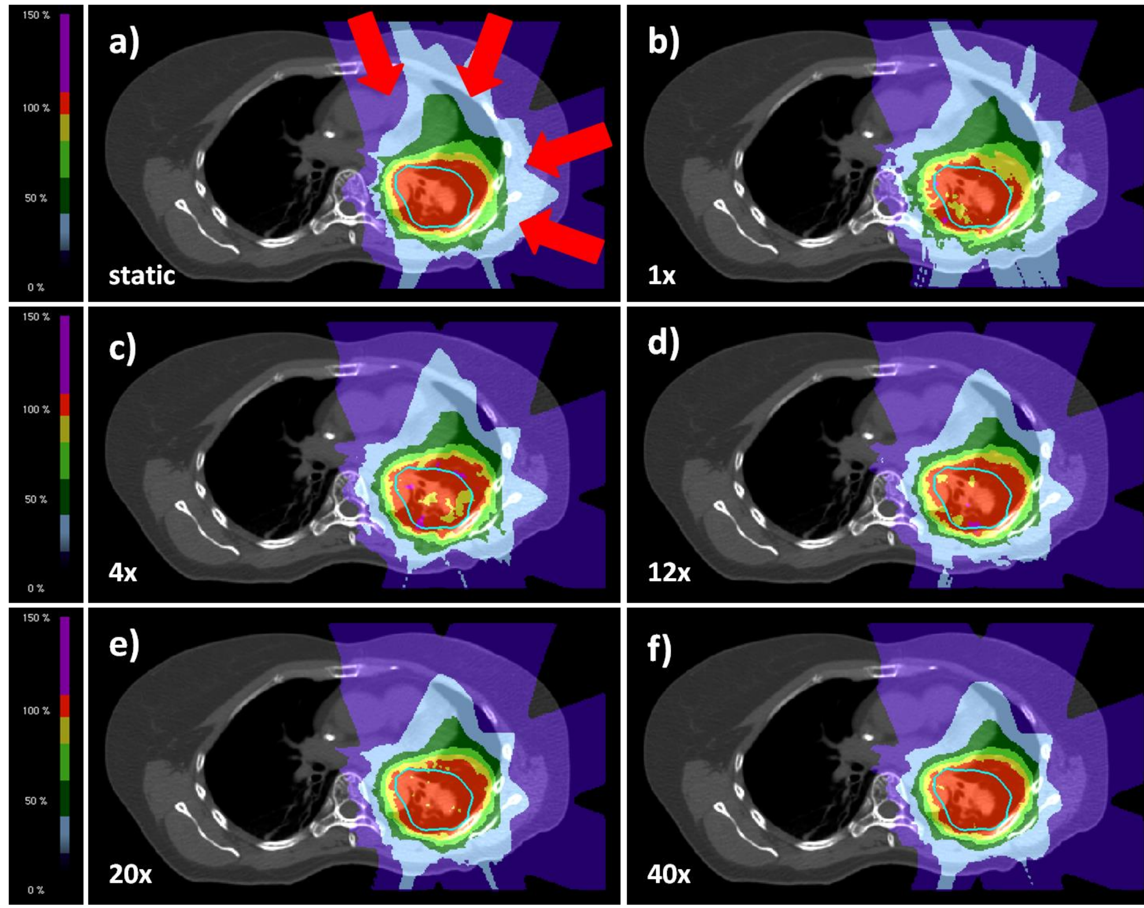


MacDonald et al, Int J Radiat Oncol Biol Phys, 1-7, 2013

Lung cancer: 2^{nd} in incidence and 1^{st} in mortality for both sexes in US



Courtesy of M. Söhn, LMU



Graeff et al., *Radiother. Oncol*. 2013

Particle therapy for atrial fibrillation

Cardiac arrhythmias

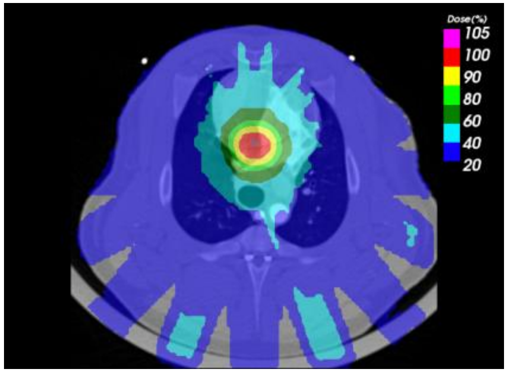
Affects about 5% of the middle-aged population and is associated with high risk of stroke and infarct

Treatment

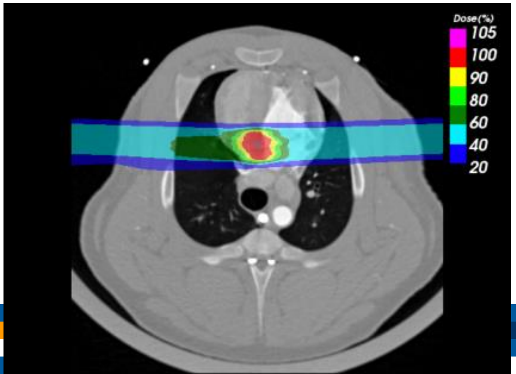
- Patients unresponsive to drugs undergo catheter ablation – very invasive, limited success
- Pre-clinical SBRT (CyberHeart, CA)

Current trial with C-ions

- First experiment in July 2013 with a pig Langedorff at HIT (Heidelberg)
- Twenty swines irradiated at GSI in July 2014

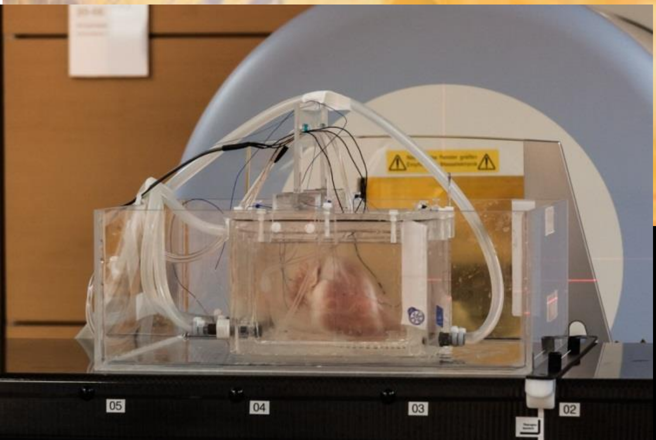


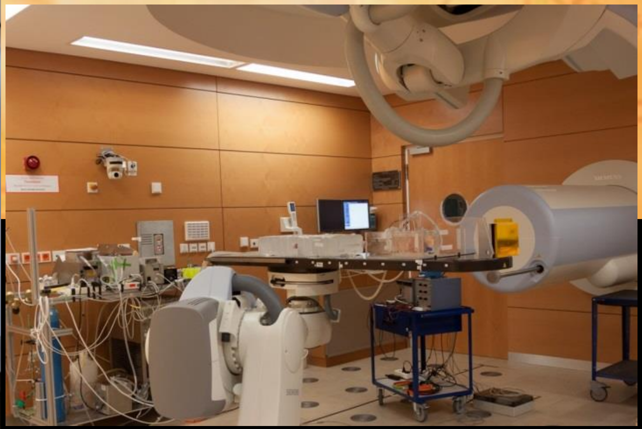
Treatment plan, X-rays



Treatment plan, C-ions

GSI MAYO CLINIC Heidelberg University Hospital

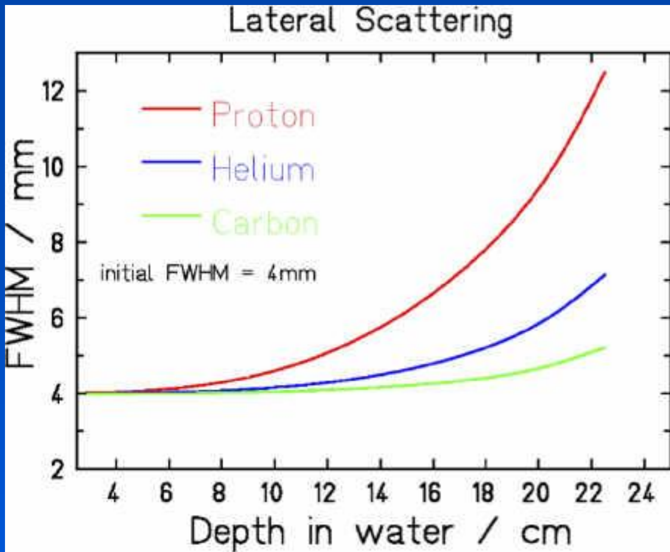




HIT
Heidelberger Ionenstrahl-Therapiezentrum

Langendorff, July 2013

4. Other Ions: Helium and Oxygen

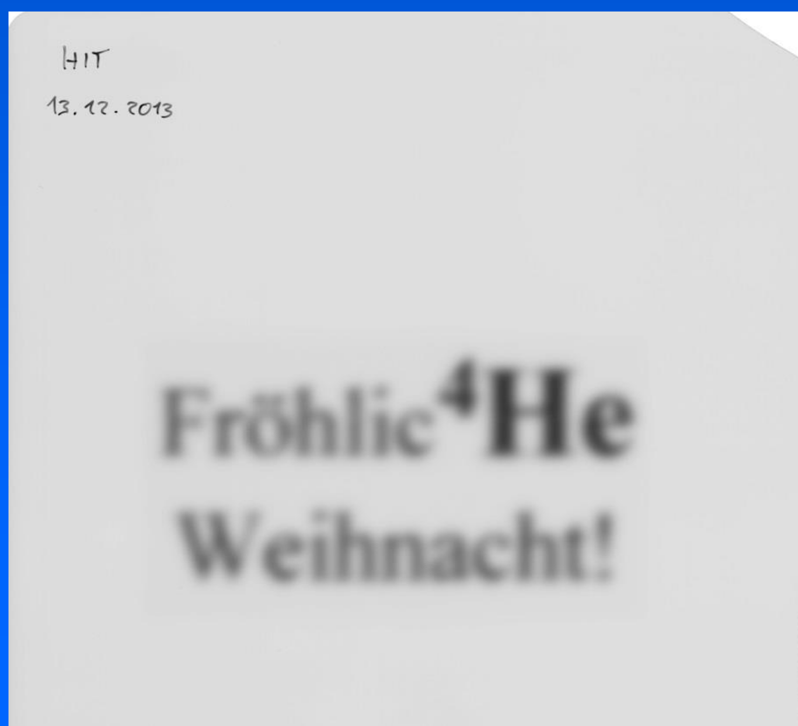


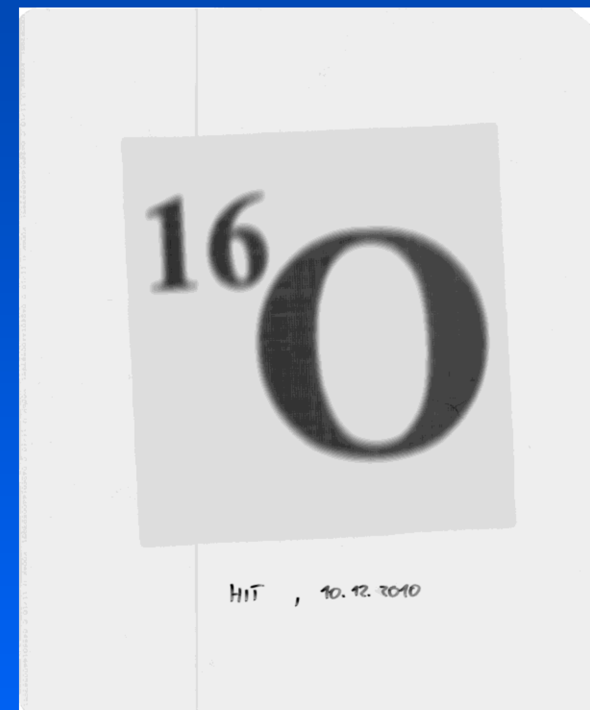
Penumbra comparison (90% => 10%):

Protons: 17,4 mm

Helium4: 10,9 mm

Carbon: 7,4 mm





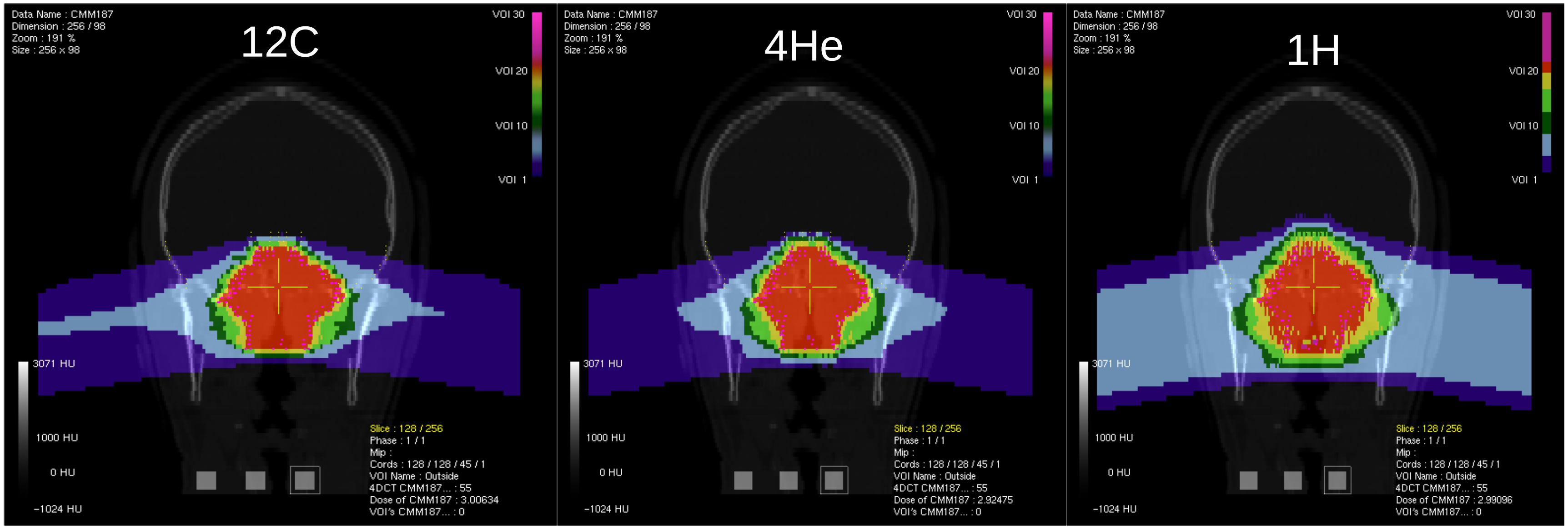
Rasterscan @ HIT-R+D-Cave

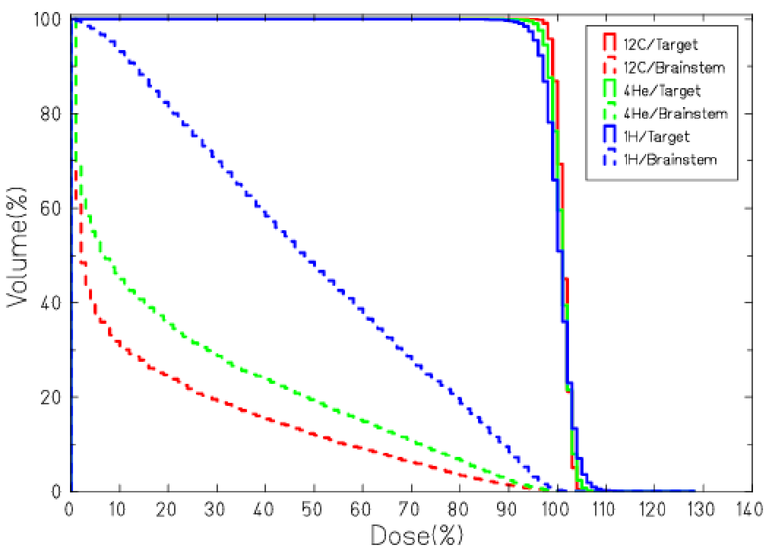
Courtesy of Thomas Haberer, HIT

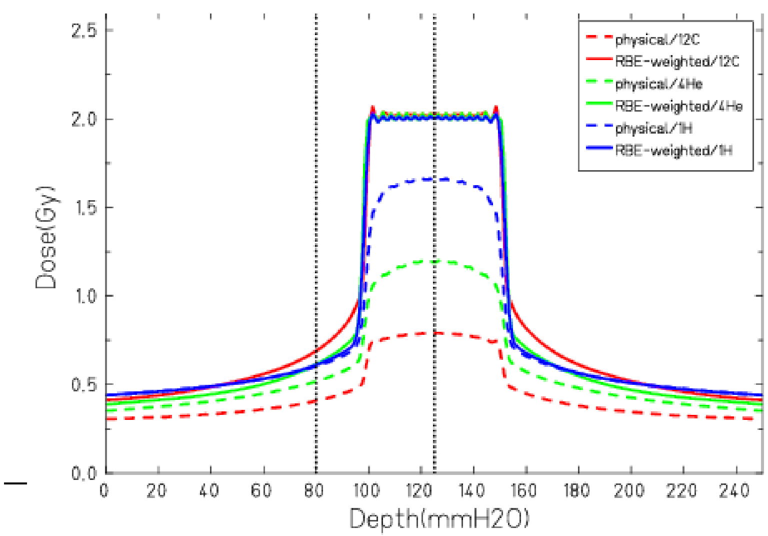
Helium TP simulation

Skull base chordoma, α/β=2 Gy

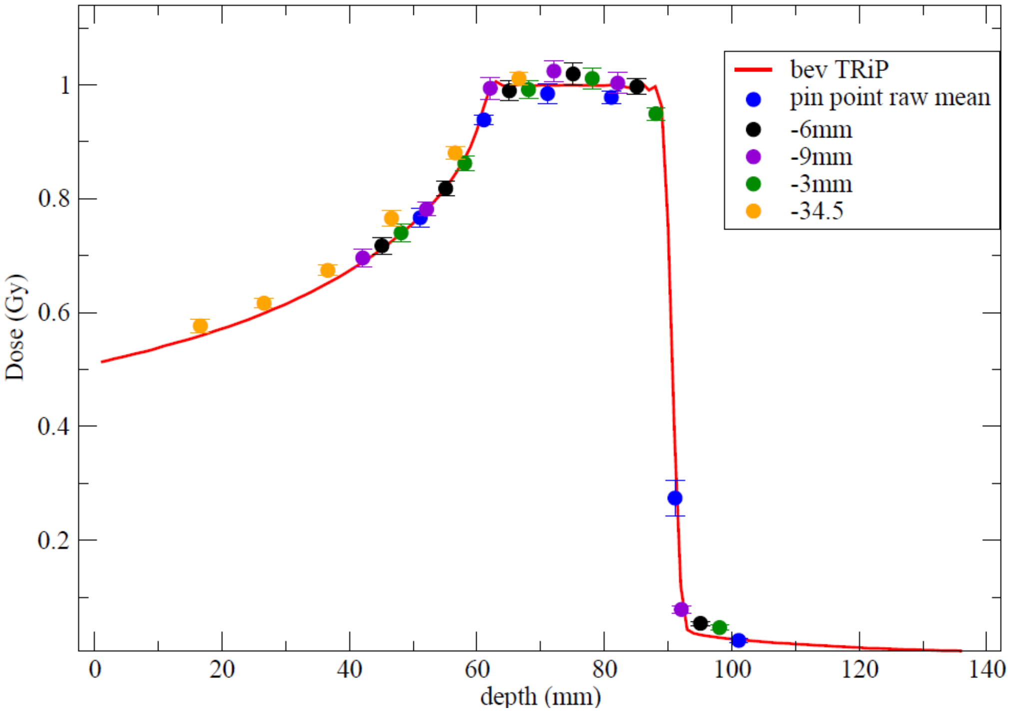
Grün et al., GSI Rep. 2014

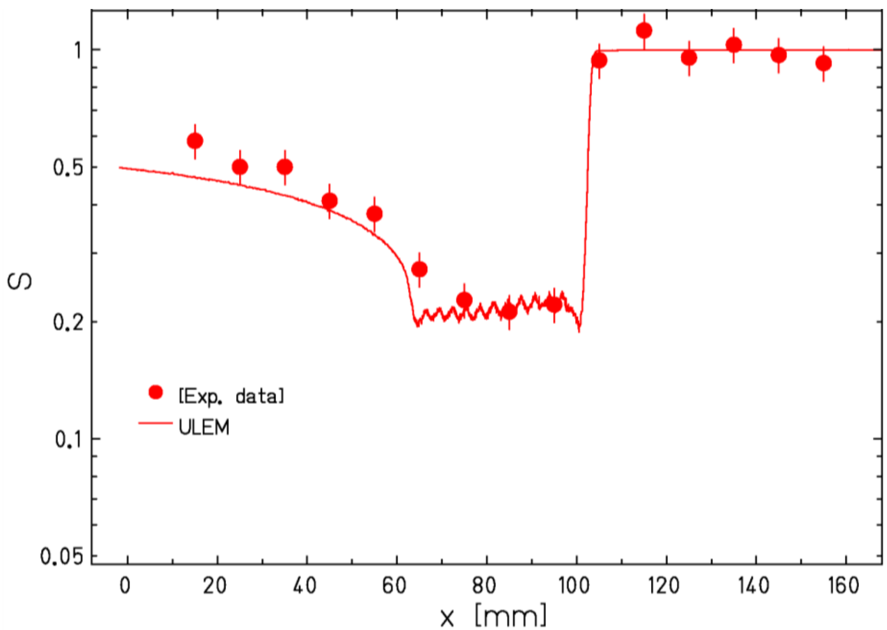






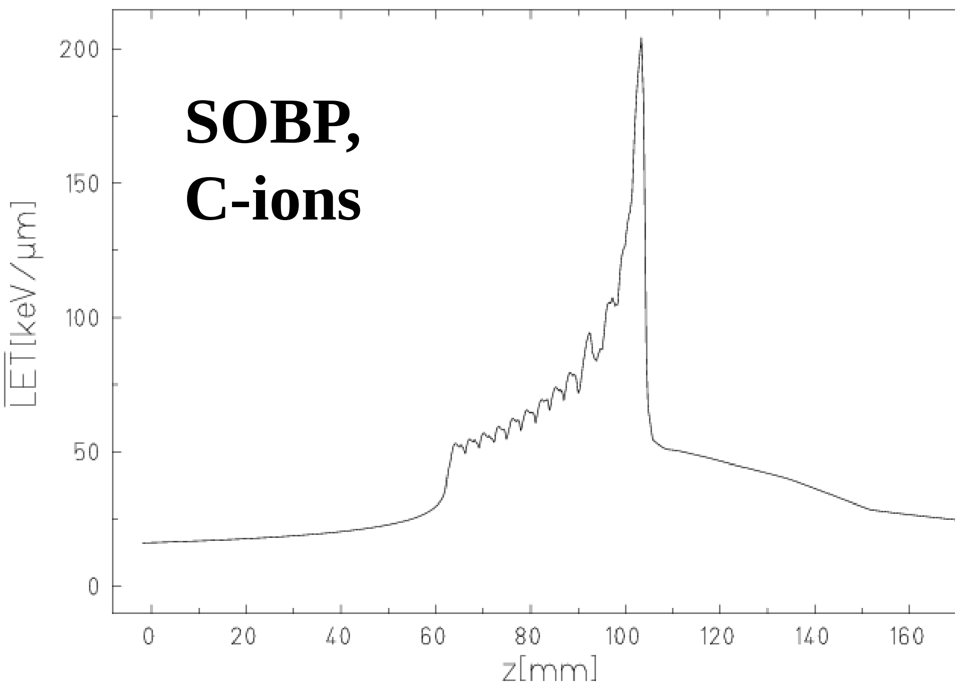
Helium: pre-clinical experimental studies

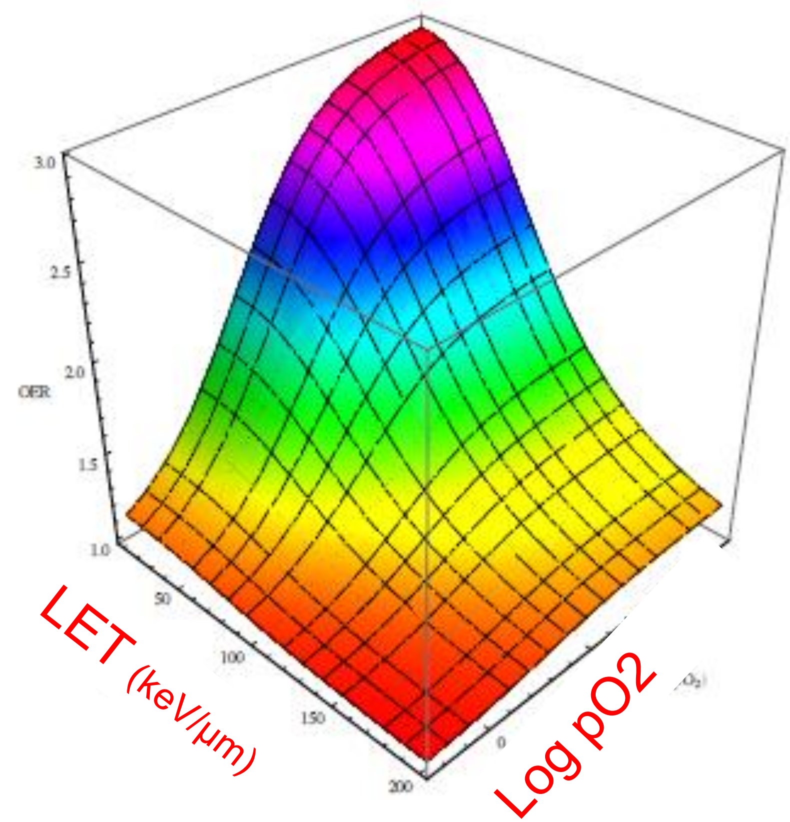




SOBP, He-ions
Krämer *et al.*, GSI Report 2014

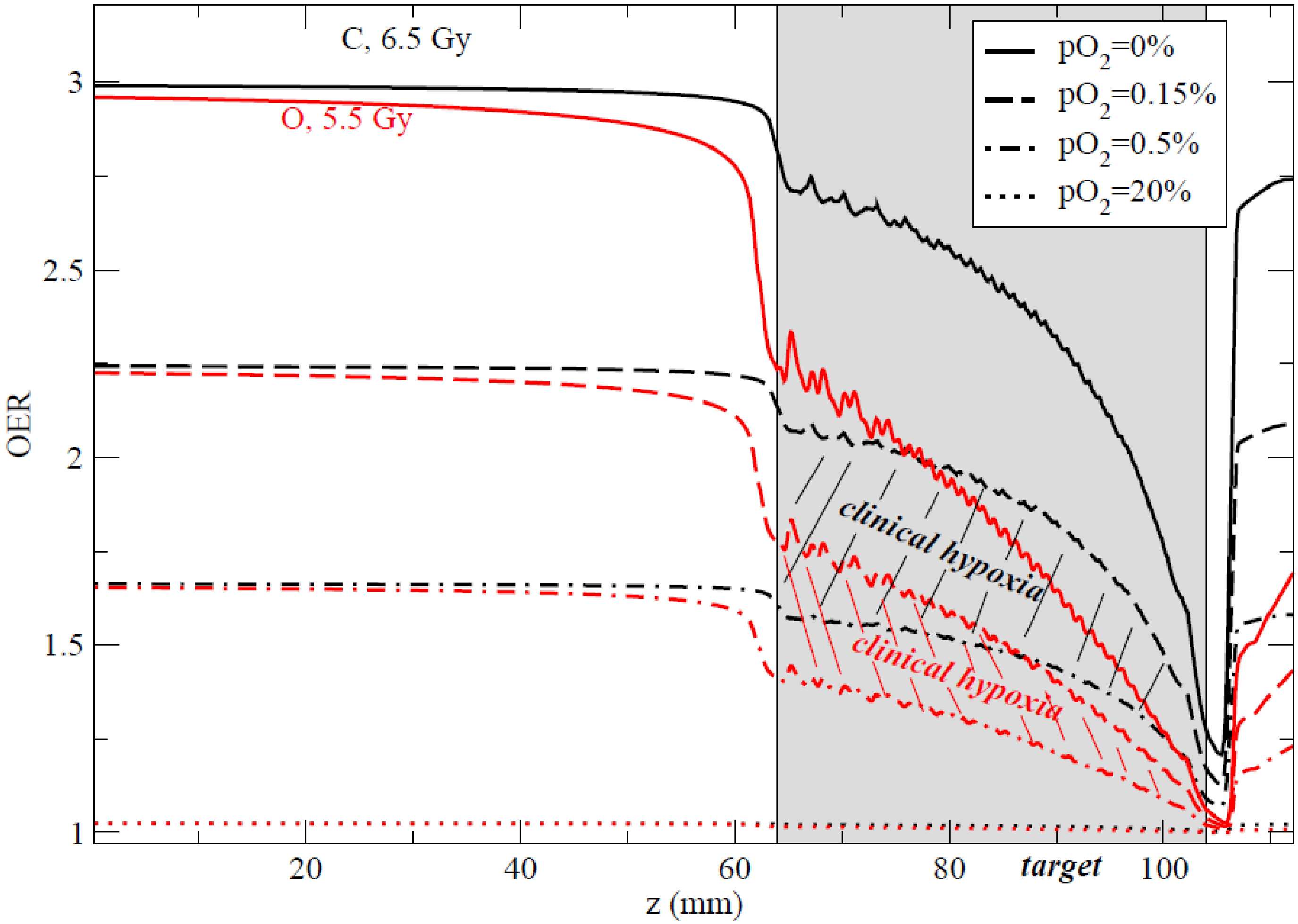
OER(pO_2, LET) model for adaptive particle treatment planning





Scifoni *et al., Phys. Med. Biol*. 2013

New ions: oxygen

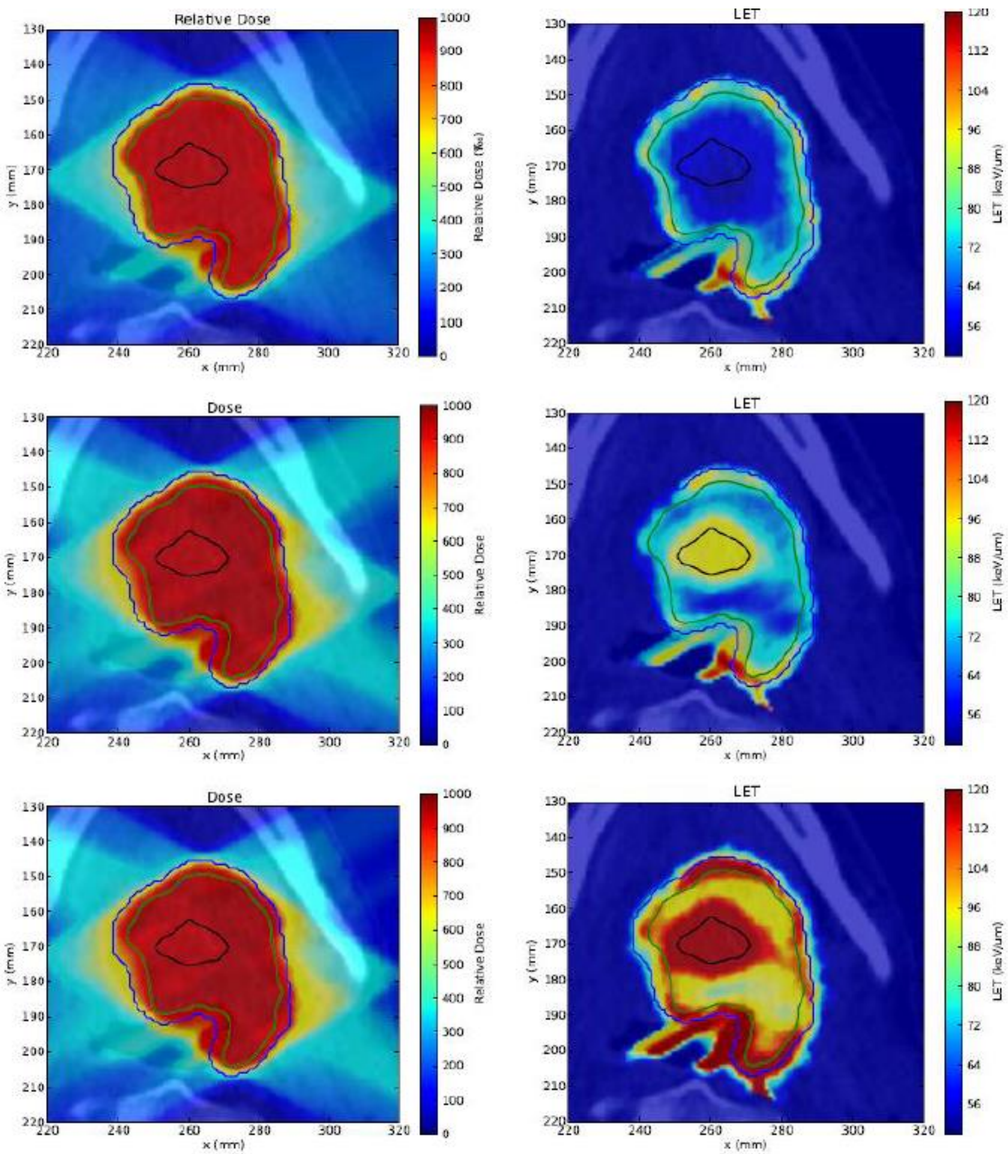


Krämer *et al., J. Phys. Chem. Solids* 2013

- C, O, p and soon He available @HIT
- Joining OER driven and Multiion modality in next TRiP release

LET painting

Bassler *et al.*, *Acta Oncol*. 2013



4 flat fields C-ions

4 ramped fields C-ions

4 ramped fields O-ions

Conclusions

- The future of particle therapy strongly depends on improvements in medical physics
- Reduction of range uncertainty is mandatory and strategies beyond fiducial markers and gating/rescanning should be found (tracking, online monitoring, proton radiography)
- Beam deliver technologies (including 4D/5D optimization) to broaden the diseases elected to be treated with particles is very important to reduce the cost/benefit ratio of the facility
- New ions can be use for pediatrics (^{4}He) or very hypoxic tumors in single-fractions (^{16}O) but require preliminary nuclear physics measurements (attenuation, fragmentation)
- BNL would be the ideal facility for this research, urgently needed in US in relation to the NCI P20 now ready to start

Biophysics Department

- M. Durante (Director)
- G. Kraft (Helmholtz Professor)
- G. Taucher-Scholz (DNA damage)
- S. Ritter (Stem cells)
- C. Fournier (Late effects)
- W. Kraft-Weyrather (Clinical radiobiology)
- M. Scholz (Biophysical modelling)
- M. Krämer (Treatment planning)
- C. Bert (Moving targets)
- C. La Tessa (Dosimetry)

Thank you very much!

http://www.gsi.de/biophysik/